CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA
Bromadiolone

Chemical Code # 0002135, Tolerance # 60235
SB 950 # 499
Original date 3/5/97

I. DATA GAP STATUS

Chronic toxicity, rat:	No study on file.
Chronic toxicity, dog:	No study on file.
Oncogenicity, rat:	No study on file.
Oncogenicity, mouse:	No study on file.
Reproduction, rat:	No study on file.
Teratology, rat:	Data gap, inadequate study, no adverse effect indicated
Teratology, rabbit:	Data gap, inadequate study, no adverse effect indicated
Gene mutation:	No data gap, possible adverse effect
Chromosome effects:	No data gap, no adverse effect
DNA damage:	No data gap, no adverse effect
Neurotoxicity:	Not required at this time

Toxicology one-liners are attached.

All record numbers through 126412 were examined.
** indicates an acceptable study.
Bold face indicates a possible adverse effect.
indicates a study on file but not yet reviewed.
File name: T970313
Assembled by H. Green, 3/5/97, and J. Gee, 3/13/97

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

COMBINED, RAT

No study on file.

CHRONIC TOXICITY, RAT

No study on file.

CHRONIC TOXICITY, DOG

No study on file.

ONCOGENICITY, RAT

No study on file.

ONCOGENICITY, MOUSE

No study on file.

REPRODUCTION, RAT

No study on file.

TERATOLOGY, RAT

017, 007 114780, 038046, "Teratology Study in the Rat with LM 637 - Bromadiolone", (G. Monnot, et al, Institut Francais de Researches et Essais Biologiques, Domaine des Oncins, BP109-692101'Arborasle, France, Report # 105204, Original Date: 6 May 1981; reformatted 17 February 1990). 25 inseminated OFA Sprague-Dawley female rats per group received 0 (aqueous polyethylene glycol), 17.5, 35.0, and 70.0 µg/kg/day of bromadiolone technical (99.8% purity) by gavage on gestation days 6 through 15. 12 of the 25 dams in the 70.0 µg/kg/day group died between gestation days 15 to 19. Maternal NOEL = 35.0 µg/kg/day. Developmental NOEL = 70.0 µg/kg/day. **Teratogenicity is not indicated**. **Unacceptable** and upgradeable (dosing solution analyses). (H. Green, 8/1/96, and J. Gee, 3/12/97).

TERATOLOGY, RABBIT

018, 007 114781, 038047, "Teratology Study in the Rabbit with LM 637, Bromadiolone", (Ph. Briet, et. al., Institut Francais de Researches et Essais Biologiques, Domaines des Oncins, BP109-692101'Arboasle, France, Report # 106206, Original study date: 3 June 1981. Reformatted 29 March 1990). 19 or 20 inseminated New Zealand White female rabbits received 0 (aqueous polyethylene glycol), 2, 4, and 8 µg/kg/day of bromadiolone technical (99.8% purity) by gavage on gestation days 6 through 18. Vaginal bleeding was noted in 8 high dose dams. Maternal NOEL = 4 µg/kg/day. Mean fetal weights were reduced at 8 µg/kg/day. Developmental NOEL = 4 µg/kg/day. **Teratogenicity is not indicated**. **Unacceptable** and not upgradeable. (All fetuses were not evaluated for both skeletal and visceral changes, no analysis of dosing material). (H. Green, 8/9/96, and J. Gee, 3/12/97).

GENE MUTATION

****016 114776**, "Test to Evaluate the Induction of Genic Mutations in CHO Cells (HGPRT Locus), Bromadiolone", (Nicole Weill, Hazleton France, Les Oncins BP 0118, 69593 L'Arbresle Cedex, France, Report # 006300, 10 July 1990). The test article is identified as bromadiolone. Chinese hamster ovary cells (CHO-K1-BH4) were exposed in duplicate in the presence and absence of activation to bromadiolone concentrations of 0 (DMSO), 5×10^{-3}, 10^{-2}, 5×10^{-2}, 10^{-1}, and 2×10^{-1} mg/ml for 4 hours in two trials, 12 dishes per concentration for mutants. **An increase in mutations under activated conditions is indicated at 10^{-1} mg/ml only in both trials**. **Acceptable**. (H. Green, 2/19/97, and J. Gee, 3/11/97).

025 126410, "Mutagenicity Test on Bromadiolone Technical in the CHO/HGPRT Forward Mutation Assay", (Maria A. Ciofone, Hazleton Washingtion, Inc., Report # 15310-0-435, 13 July 1993). The test article is identified as bromadiolone technical with 98% purity. Chinese hamster ovary cells (CHO-K1-BH4) were exposed for 4 hours to bromadiolone concentrations of 0, 10, 20, 40, 60, 80, and 90 µg/ml with activation and to 0, 20, 40, 60, 80, 100, 125, and 150 µg/ml without. **An increase in forward mutations is not indicated. **Acceptable**. (H. Green, 1/28/97, and J. Gee, 3/12/97).

CHROMOSOME EFFECTS

016 114777, "Test to Evaluate the Ability to Induce Chromosome Aberrations in Human Lymphocytes (LYMP.)", (Nicole Weill, Hazleton France, Les Oncins, B.P. 0118, 69593 L'Arbresle Cedex, France, Report # 006328, 9 July 1990). Human lymphocytes in whole blood were exposed in duplicate to bromadiolone (Maki technical, 98.95% purity) concentrations of 0 (DMSO), 5×10^{-2}, 10^{-1}, and 2×10^{-1} mg/ml for 3 hours in the presence and absence of activation in two trials. **Induction of chromosomal aberrations is not indicated. **Acceptable.** (H. Green, 2/27/97, and J. Gee, 3/11/97).

016 114779, "Research Report on the Assessment of the *In Vivo* Mutagenicity of Bromadiolone Using the Micronucleus Test", (X.Fouillet and D. Gutty, Batelle, Geneva Research Centres, 7, route de Drize, 1227 Carouge-Geneve, Switzerland, Report # 7270 03, October 1981). 3 OF-1 albino mice per sex per group received 2 intragastric intubations (24-hour interval between administrations) of bromadiolone (99.8% purity) at concentrations of 0, 2, and 200 mg/kg. Bone marrow was sampled 6 hours after the second intubation. **An increase in micronucleated polychromatic erythrocytes is not indicated. Unacceptable** and not upgradeable (too few animals per group, inadequate bone marrow sampling time, no justification for dosing levels). (H. Green, 2/28/97, and J. Gee, 3/11/97).

025 126412, "Mutagenicity Test on Bromadiolone Technical in an <u>In Vitro</u> Cytogenetic Assay Measuring Chromosomal Aberrations in Human Whole Blood Lymphocytes: With and Without Exogenous Metabolic Activation", (Hemalatha Murli, Ph.D., Hazleton Washington, Inc., 9200 Leesburg Pike, Vienna, VA., Report # 15310-0-449, 1 July 1993. Human whole blood lymphocytes were exposed in duplicate for 2 hours to bromadiolone technical (98.72% purity) in the presence of activation at 0, 37.5, 50.0, 74.9, and 99.9 µg/ml and for 26.1 hours in the absence of activation at concentrations of 0, 7.49, 9.99, 25.0, 50.0, and 74.9 µg/ml. **An increase in chromosomal aberrations is not indicated. **Acceptable**. (H. Green, 2/7/97, and J. Gee, 3/12/97).

DNA DAMAGE

025 126411, "Mutagenicity Test on Bromadiolone, Technical in An *In Vivo* Mouse Micronucleus Assay", (Hemalatha Murli, Ph.D., Hazleton Washington, Inc., 9200 Leesburg Pike, Vienna, VA., Report # 15310-0-455, 12 July 1993). 5 vehicle control and 20 treated ICR mice per sex per group received intraperitoneal injections of bromadiolone technical (98.72% purity) at 0 (corn oil) and 400 mg/kg/day respectively for 3 days. Bone marrow was sampled 24 hours after the final treatment. **Increased frequency of micronucleated polychromatic erythrocytes is not indicated. Acceptable. (H. Green, 1/31/97, and J. Gee, 3/12/97).